

The United States **Pharmacopeia**

TWENTIETH REVISION

Official from July 1, 1980

The National **Formulary**

FIFTEENTH EDITION

Official from July 1, 1980

United States Pharmacopeial Convention, Inc.
12601 Twinbrook Parkway, Rockville, Md. 20852



Labeling—Label it to indicate its viscosity type [viscosity of a solution (1 in 50)].

Other requirements—It responds to the *Identification tests* and meets the requirements for *Apparent viscosity*, *Loss on drying*, *Residue on ignition*, *Arsenic*, and *Heavy metals* under *Hydroxypropyl Methylcellulose 2906*.

Assay—Proceed as directed in the *Assay* under *Hydroxypropyl Methylcellulose 2906*, except to substitute Hydroxypropyl Methylcellulose 1828 for Hydroxypropyl Methylcellulose 2906 throughout.

Hydroxypropyl Methylcellulose 2208

Cellulose, 2-hydroxypropyl methyl ether.

Cellulose hydroxypropyl methyl ether [9004-65-3].

» Hydroxypropyl Methylcellulose 2208 is a propylene glycol ether of methylcellulose. It contains not less than 19.0 percent and not more than 24.0 percent of methoxy ($-\text{OCH}_3$), and not less than 4.0 percent and not more than 12.0 percent of hydroxypropoxy ($-\text{OCH}_2\text{CHOHCH}_3$), calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate its viscosity type [viscosity of a solution (1 in 50)].

Other requirements—It responds to the *Identification tests* and meets the requirements for *Apparent viscosity*, *Loss on drying*, *Residue on ignition*, *Arsenic*, and *Heavy metals* under *Hydroxypropyl Methylcellulose 2906*.

Assay—Proceed as directed in the *Assay* under *Hydroxypropyl Methylcellulose 2906*, except to substitute Hydroxypropyl Methylcellulose 2208 for Hydroxypropyl Methylcellulose 2906 throughout.

Hydroxypropyl Methylcellulose 2906

Cellulose, 2-hydroxypropyl methyl ether.

Cellulose hydroxypropyl methyl ether [9004-65-3].

» Hydroxypropyl Methylcellulose 2906 is a propylene glycol ether of methylcellulose. It contains not less than 27.0 percent and not more than 30.0 percent of methoxy ($-\text{OCH}_3$), and not less than 4.0 percent and not more than 7.5 percent of hydroxypropoxy ($-\text{OCH}_2\text{CHOHCH}_3$), calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate its viscosity type [viscosity of a solution (1 in 50)].

Identification—

A: Gently add 1 g to the top of 100 ml of water in a beaker, and allow to disperse over the surface, tapping the top of the container to ensure an even dispersion of the substance. Allow the beaker to stand until the substance becomes transparent and mucilaginous (about 5 hours), and swirl the beaker to wet the remaining substance, add a stirring bar, and stir until solution is complete: the mixture remains stable when an equal volume of 1 N sodium hydroxide or 1 N hydrochloric acid is added.

B: Add 1 g to 100 ml of boiling water, and stir the mixture: a slurry is formed, but the powdered material does not dissolve. Cool the slurry to 20° and stir: the resulting liquid is a clear or opalescent mucilaginous colloidal mixture.

C: Pour a few ml of the mixture prepared for *Identification test B* onto a glass plate, and allow the water to evaporate: a thin, self-sustaining film results.

Apparent viscosity—Proceed as directed in the test for *Apparent viscosity* under *Methylcellulose*. Its viscosity is not less than 80.0% and not more than 120.0% of that stated on the label for viscosity types of 100 centipoises or less; and not less than 75.0% and not more than 140.0% of that stated on the label for viscosity types higher than 100 centipoises.

Loss on drying (731)—Dry it at 105° for 2 hours: it loses not more than 5.0% of its weight.

Residue on ignition (281): not more than 1.5% for Hydroxypropyl Methylcellulose 2906 having a labeled viscosity of greater than 30 centipoises, and not more than 3% for Hydroxypropyl Methylcellulose 2906 having a labeled viscosity of 50 centipoises or less.

Arsenic (211): 3 ppm.

Heavy metals (231)—Determine as directed in the test for *Heavy metals* under *Methylcellulose*: the limit is 0.001%.

Assay—[Caution—Perform all steps involving hydriodic acid carefully, in a well-ventilated hood. Use goggles, acid-resistant gloves, and other appropriate safety equipment. Be exceedingly careful when handling the hot vials, since they are under pressure. In the event of hydriodic acid exposure, wash with copious amounts of water, and seek medical attention at once.]

Internal standard solution—Transfer about 2.5 g of toluene, accurately weighed, to a 100-ml volumetric flask containing 10 ml of *o*-xylene, dilute with *o*-xylene to volume, and mix.

Standard preparation—Into a suitable serum vial weigh about 135 mg of adipic acid and 4.0 ml of hydriodic acid, pipet 4 ml of *Internal standard solution* into the vial, and close the vial securely with a suitable septum stopper. Weigh the vial and contents accurately, add 30 μ l of isopropyl iodide through the septum with a syringe, again weigh, and calculate the weight of isopropyl iodide added, by difference. Add 90 μ l of methyl iodide similarly, again weigh, and calculate the weight of methyl iodide added, by difference. Shake well, and allow the layers to separate.

Assay preparation—Transfer about 0.065 g of dried Hydroxypropyl Methylcellulose 2906, accurately weighed, to a suitable 5-ml vial equipped with a pressure-tight septum-type closure, add an amount of adipic acid equal to the weight of the test specimen, and pipet 2 ml of *Internal standard solution* into the vial. Cautiously pipet 2 ml of hydriodic acid into the mixture, immediately cap the vial tightly, and weigh accurately. Shake the vial for 30 seconds, heat at 150° for 20 minutes, remove from the source of heat, wrap in a towel, shake again, using extreme caution, and heat at 150° for an additional 40 minutes. Allow the vial to cool for about 45 minutes, and again weigh. If the weight loss is greater than 10 mg, discard the mixture, and prepare another *Assay preparation*.

Chromatographic system—Use a gas chromatograph equipped with a thermal conductivity detector. Under typical conditions, the instrument contains a 1.8-m X 4-mm glass column packed with 10 percent liquid phase G1 on 100- to 120-mesh support S1, the column is maintained at 100°, and the injection port and the detector are maintained at 200°, and helium is used as the carrier gas at a flow rate of 20 ml per minute.

Calibration—Inject about 2 μ l of the upper layer of the *Standard preparation* into the gas chromatograph, and record the chromatogram. The retention times for methyl iodide, isopropyl iodide, toluene, and *o*-xylene are approximately 3, 5, 7, and 13 minutes, respectively. Calculate the relative response factor, F_{mi} , of equal weights of toluene and methyl iodide by the formula Q_{mi}/A_{mi} , in which Q_{mi} is the quantity ratio of methyl iodide to toluene in the *Standard preparation*, and A_{mi} is the peak area ratio of methyl iodide to toluene obtained from the *Standard preparation*. Similarly, calculate the relative response factor, F_{ii} , of equal weights of toluene and isopropyl iodide by the formula Q_{ii}/A_{ii} , in which Q_{ii} is the quantity ratio of isopropyl iodide to toluene in the *Standard preparation*, and A_{ii} is the peak area ratio of isopropyl iodide to toluene obtained from the *Standard preparation*.

Procedure—Inject about 2 μ l of the upper layer of the *Assay preparation* into the gas chromatograph, and record the chromatogram. Calculate the percentage of methoxy in the Hydroxypropyl Methylcellulose 2906 by the formula $2(31/142) F_{mi} A_{umi} (W_i/W_u)$, in which 31/142 is the ratio of the formula weights of methoxy and methyl iodide, F_{mi} is defined under *Calibration*, A_{umi} is the ratio of the area of the methyl iodide peak to that of the toluene peak obtained from the *Assay preparation*, W_i is the weight, in g, of toluene in the *Internal standard solution*, and W_u is the weight, in g, of Hydroxypropyl Methylcellulose 2906 taken for the *Assay*. Similarly, calculate the percentage of hydroxypropoxy in the Hydroxypropyl Methylcellulose 2906 by the formula $2(75/170) F_{ii} A_{uii} (W_i/W_u)$, in which 75/170 is the ratio of the formula weights of hydroxypropoxy and isopropyl iodide, F_{ii} is defined under *Calibration*, A_{uii} is the ratio of the area of the isopropyl iodide peak to that of the toluene peak obtained from the *Assay preparation*, W_i is the weight, in g, of toluene in the *Internal standard solution*, and W_u is the weight, in g, of Hydroxypropyl Methylcellulose 2906 taken for the *Assay*.

388 Hydroxypropyl / Official Monographs

USP XX

Hydroxypropyl Methylcellulose 2910

Cellulose, 2-hydroxypropyl methyl ether.
Cellulose hydroxypropyl methyl ether. [9004-65-3].

» Hydroxypropyl Methylcellulose 2910 is a propylene glycol ether of methylcellulose. It contains not less than 28.0 percent and not more than 30.0 percent of methoxy ($-\text{OCH}_3$), and not less than 7.0 percent and not more than 12.0 percent of hydroxypropoxy ($-\text{OCH}_2\text{CHOHCH}_3$), calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate its viscosity type [viscosity of a solution (1 in 50)].

Other requirements—It responds to the *Identification tests* and meets the requirements for *Apparent viscosity*, *Loss on drying*, *Residue on ignition*, *Arsenic*, and *Heavy metals* under *Hydroxypropyl Methylcellulose 2906*.

Assay—Proceed as directed in the *Assay* under *Hydroxypropyl Methylcellulose 2906*, except to substitute Hydroxypropyl Methylcellulose 2910 for Hydroxypropyl Methylcellulose 2906 throughout.

Hydroxypropyl Methylcellulose Ophthalmic Solution

» Hydroxypropyl Methylcellulose Ophthalmic Solution is a sterile solution of Hydroxypropyl Methylcellulose. It contains not less than 85.0 percent and not more than 115.0 percent of the labeled amount of hydroxypropyl methylcellulose of a grade containing not less than 19.0 percent and not more than 30.0 percent of methoxy ($-\text{OCH}_3$) and not less than 4.0 percent and not more than 12.0 percent of hydroxypropoxy ($-\text{OCH}_2\text{CHOHCH}_3$), calculated on the dried basis. It may contain suitable antimicrobial, buffering, and stabilizing agents.

Packaging and storage—Preserve in tight containers.

Reference standard—USP Hydroxypropyl Methylcellulose Reference Standard—Dry at 105° for 2 hours before using.

Identification—

A: It responds to *Identification test C* under *Hydroxypropyl Methylcellulose*.

B: Heat 5 ml of Ophthalmic Solution in a test tube over a low flame: the warm solution turns cloudy but clears upon chilling.

Sterility—It meets the requirements under *Sterility Tests* (71).

pH (791): between 6.0 and 7.8.

Assay—

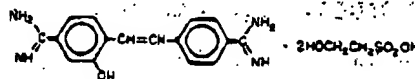
Standard preparation—Dissolve a suitable quantity of USP Hydroxypropyl Methylcellulose RS, accurately weighed, in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 100 µg per ml.

Assay preparation—Dilute quantitatively an accurately measured volume of Hydroxypropyl Methylcellulose Ophthalmic Solution with water to obtain a solution having an equivalent concentration of approximately 100 µg of hydroxypropyl methylcellulose per ml.

Procedure—Pipet 2 ml each of the *Standard preparation*, the *Assay preparation*, and water to provide a blank, into separate, glass-stoppered test tubes. To each tube add 5.0 ml of diphenylamine solution (prepared by dissolving 3.75 g of colorless diphenylamine crystals in 150 ml of glacial acetic acid and diluting the solution with 90 ml of hydrochloric acid), mix, and immediately insert the tubes into an oil bath at 105° to 110° for 30 minutes, the temperature being kept uniform within 0.1° during heating. Remove the tubes, and place them in an ice-water bath for 10 minutes or until thoroughly cool. Concomitantly determine, at room temperature, the absorbances of the solutions from the *Standard preparation* and the *Assay preparation* at 635 nm, with a suitable

spectrophotometer, using the water solution as the blank. Calculate the quantity, in mg, of hydroxypropyl methylcellulose in each ml of the Ophthalmic Solution by the formula $0.001C(d/V)(A_U/A_S)$, in which C is the concentration, in µg per ml, of USP Hydroxypropyl Methylcellulose RS in the Standard solution, d is the dilution fold of V used to obtain the *Assay preparation*, V is the volume, in ml, of Ophthalmic Solution taken, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxystilbamidine Isethionate



$\text{C}_{16}\text{H}_{16}\text{N}_4\text{O} \cdot 2\text{C}_2\text{H}_6\text{O}_4\text{S}$ 532.58
Benzencarboximidamide, 4-[2-(4-(aminiminomethyl)phenyl)-ethenyl]-3-hydroxy-, bis(2-hydroxyethanesulfonate) (salt).
2-Hydroxy-4,4'-stilbenedicarboximidine bis(2-hydroxyethanesulfonate) (salt). [533-22-2].

» Hydroxystilbamidine Isethionate contains not less than 97.0 percent and not more than 103.0 percent of $\text{C}_{16}\text{H}_{16}\text{N}_4\text{O} \cdot 2\text{C}_2\text{H}_6\text{O}_4\text{S}$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

Reference standard—USP Hydroxystilbamidine Isethionate Reference Standard—Dry in vacuum at 60° for 3 hours before using.

Identification—

A: The infrared absorption spectrum of a potassium bromide dispersion of it, previously dried, exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydroxystilbamidine Isethionate RS.

B: The ultraviolet absorption spectrum of a 1 in 100,000 solution in 0.01 N hydrochloric acid exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Hydroxystilbamidine Isethionate RS, concomitantly measured.

pH (791): between 4.0 and 5.5; in a solution (1 in 100).

Loss on drying (731)—Dry about 200 mg, accurately weighed, in vacuum at 60° for 3 hours; it loses not more than 1.0% of its weight.

Residue on ignition (281): not more than 0.1%, 2 g being used for the test.

Selenium (291): 0.003%, a 200-mg test specimen being used.

Heavy metals, Method II (231): 0.001%.

Assay—Transfer about 100 mg of Hydroxystilbamidine Isethionate, accurately weighed, to a titration vessel, dissolve in 25 ml of water, and add 100 ml of hydrochloric acid. Titrate the solution with 0.1 N bromine VS, determining the end-point potentiometrically, using platinum-calomel electrodes. Each ml of 0.1 N bromine is equivalent to 26.63 mg of $\text{C}_{16}\text{H}_{16}\text{N}_4\text{O} \cdot 2\text{C}_2\text{H}_6\text{O}_4\text{S}$.

Sterile Hydroxystilbamidine Isethionate

» Sterile Hydroxystilbamidine Isethionate is Hydroxystilbamidine Isethionate suitable for parenteral use.

Packaging and storage—Preserve in light-resistant Containers for Sterile Solids as described under *Injections* (1).

Reference standard—USP Hydroxystilbamidine Isethionate Reference Standard—Dry in vacuum at 60° for 3 hours before using.

Completeness of solution (641)—The contents of 1 container dissolve in 10 ml of carbon dioxide-free water to yield a clear solution.

Constituted solution—At the time of use, the constituted solution prepared from Sterile Hydroxystilbamidine Isethionate meets the requirements for *Constituted Solutions* under *Injections* (1).

METHOCEL
PREMIUM CELLULOSE ETHERS

PRODUCT SPECIFICATIONS

METHOCEL K100M Premium EP

is hydroxypropyl methylcellulose 2208 (hypromellose) which meets the requirements of the United States Pharmacopoeia XXIV and European Pharmacopoeia 3rd edition and is certified Kosher.

- METHOCEL Premium HPMC polymers can be used in controlled release hydrophilic matrix systems and controlled release coatings, as granulation binders, and as viscosity modifiers and suspending agents in liquid systems.

□ Particle Size

- Minimum 99.0% through No. 40 US standard sieve.

□ Shelf Life

- The material has a recommended shelf life of five years from the date of manufacture if stored in well closed containers.

□ Packaging

- 25 kg polylined fibre drums.

Test Items Specifications

Description: White to slightly off white, fibrous or granular powder

Identity: Meets the requirements of the USP and PhEur

Appearance of solution: Less coloured than reference solution Y₆ and less opalescent than reference suspension III

pH
(1% solution): 5.5-8.0

Methoxyl content: 19.0-24.0%

Hydroxypropoxyl content: 7.0-12.0%

Apparent viscosity: 16922-19267 mPa.s
(nominal value 18243 mPa.s) by rotation

Apparent viscosity: 80000-120000 cP (nominal value 100000 cP) by Ubbelohde

Chlorides: max 0.5%

Heavy Metals: max 10ppm as Pb

Loss on drying: max 5.0%

Sulphated Ash: max 1.0%

Organic Volatile Impurities: will pass USP test <467>

MYPS/TF10824/09/00

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Colofon

METHOCEL
PREMIUM CELLULOSE ETHERS

PRODUCT SPECIFICATIONS

METHOCEL ES Premium LV EP

is hydroxypropyl methylcellulose 2910 (hypromellose) which meets the requirements of the United States Pharmacopoeia XXIV and European Pharmacopoeia 3rd edition and is certified Kosher.

- ☐ METHOCEL Premium HPMC polymers can be used in controlled release hydrophilic matrix systems and controlled release coatings, as granulation binders, and as viscosity modifiers and suspending agents in liquid systems.

- ☐ Used in film-coating in the form of Opadry®.

☐ **Particle Size**

- Minimum 99.0% through No. 40 US standard sieve.

☐ **Shelf Life**

- The material has a recommended shelf life of five years from the date of manufacture if stored in well closed containers.

☐ **Packaging**

- 25 kg polylined fibre drums.

MEPS/TF10025/09/00

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Test Items Specifications

Description: White to slightly off white, fibrous or granular powder

Identity: Meets the requirements of the USP and PhEur

Appearance of solution: Less coloured than reference solution Y_a and less opalescent than reference suspension III

pH
(1% solution): 5.5-8.0

Methoxyl content: 28.0-30.0%

Hydroxypropoxyl content: 7.0-12.0%

Apparent viscosity: 4.2-6.1 mPa.s (nominal value 5.2 mPa.s) by rotation

Apparent viscosity: 4.0-6.0 cP (nominal value 5.0 cP) by Ubbelohde

Chlorides: max 0.5%

Heavy Metals: max 10ppm as Pb

Loss on drying: max 5.0%

Sulphated Ash: max 1.0%

Organic Volatile Impurities: will pass USP test <467%

Colorcon